Attorney Docket No: SALK3140 (088802-9803))

Application No: 10/535,042 Filing Date: January 9, 2006

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## Amendments to the Claims/Listing of Claims

Please amend claims 14, 19 and 31 as follows. This listing of claims will replace all prior versions, and listings, of claims in the application:

- (Withdrawn) A composition comprising the ligand binding domain of a farnesoid X receptor (FXR) in crystalline form.
- (Withdrawn) A composition according to claim 1 further comprising a ligand of said FXR.
- (Withdrawn) A composition according to claim 2, wherein said ligand is selected from the group consisting of fexaramine, fexarine, fexarene and GW4064.
  - 4.-5. Cancelled.
- (Withdrawn) A composition according to claim 1 as described by the structure coordinates set forth in Appendix 1, or a portion thereof sufficient to define the points of interaction between said ligand binding domain and a ligand therefor.
- (Withdrawn) A composition according to claim 2 as described by the structure coordinates set forth in Appendix 1, or a portion thereof sufficient to define the points of interaction between said ligand binding domain and said ligand.
- (Withdrawn) A composition according to claim 2, wherein the crystals belong to space group P2<sub>1</sub>2<sub>1</sub>2<sub>1</sub> with unit cell dimensions of about:

a = 37 Å, b = 57 Å, c = 117 Å,  

$$\alpha = 90^{\circ}$$
,  $\beta = 90^{\circ}$ , and  $\gamma = 90^{\circ}$ .

9 Cancelled

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 (Withdrawn) A composition according to claim 1, wherein said ligand binding domain comprises amino acid residues 248 - 476 of SEQ ID NO:1.

- 11. (Withdrawn) A computer for producing a three-dimensional representation of a farnesoid X receptor (FXR) molecule or molecular complex or a homologue of said FXR molecule or molecular complex, wherein said FXR molecule or molecular complex or a homologue of said FXR molecule or molecular complex comprises a ligand binding domain defined by structure coordinates obtained from X-ray diffraction data obtained from crystals of said FXR molecule or molecular complex or a homologue of said FXR molecule or molecular complex, said computer comprising:
  - (i) a computer-readable data storage medium comprising a data storage material encoded with computer-readable data, wherein said data comprises X-ray diffraction data obtained from crystals of said FXR molecule or molecular complex or a homologue of said FXR molecule or molecular complex;
  - (ii) a working memory for storing instructions for processing said computerreadable data:
  - (iii) a central-processing unit coupled to said working memory and to said computer-readable data storage medium for processing said computer-machine readable data into said three-dimensional representation; and
  - (iv) a display coupled to said central-processing unit for displaying said three-dimensional representation.
- (Withdrawn) A computer according to claim 11, wherein said structure coordinates are set forth in Appendix 1, or a portion thereof sufficient to define the points of interaction between said ligand binding domain and a ligand therefor.

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13. (Withdrawn) A computer for determining at least a portion of the structure coordinates corresponding to X-ray diffraction data obtained from a farnesoid X receptor (FXR) molecule or molecular complex or a homologue of said FXR molecule or molecular complex, said computer comprising:

- a computer-readable data storage medium comprising a data storage material encoded with computer-readable data, wherein said data comprises at least a portion of the structure coordinates of Appendix 1;
- (ii) a computer-readable data storage medium comprising a data storage material encoded with computer-readable data, wherein said data comprises X-ray diffraction data obtained from said FXR molecule or molecular complex or a homologue of said FXR molecule or molecular complex;
- (iii) a working memory for storing instructions for processing said computerreadable data of (i) and (ii);
- (iv) a central-processing unit coupled to said working memory and to said computer-readable data storage medium of (i) and (ii) for performing a Fourier transform of the machine readable data of (i) and for processing said computer-readable data of (ii) into structure coordinates; and
- (v) a display coupled to said central-processing unit for displaying said structure coordinates of said FXR molecule or molecular complex.
- (Currently amended) A method of predicting a molecule capable of binding to a farnesoid X receptor (FXR) molecule, said method comprising;

modeling a test molecule that potentially interacts with the composition of claim 1 a composition comprising the ligand binding domain of a farnesoid X receptor (FXR) in crystalline form, wherein said ligand binding domain is defined by a plurality of structure coordinates of the ligand binding domain of a FXR molecule or a fragment thereof,

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wherein said structure coordinates are derived from X-ray diffraction data obtained from crystals of said FXR molecule or molecular complex or a homologue of said FXR molecule or molecular complex.

 (Original) A method according to claim 14, wherein said plurality of structure coordinates are set forth in Appendix 1, or a portion thereof sufficient to define the points of interaction between said ligand binding domain and a ligand therefor.

## 16.-17. Cancelled.

- 18. (Original) A method according to claim 14, wherein said test molecule is developed using a computer algorithm to predict a three-dimensional representation of said test molecule interacting with a FXR based upon a three-dimensional representation of a FXR molecule or fragment thereof.
- (Currently amended) A method of identifying a compound with agonist, partial agonist, or antagonist activity with respect to a farnesoid X receptor (FXR) molecule, said method comprising:
  - (a) modeling a test compound that potentially interacts with the ligand binding domain of said FXR molecule or a fragment thereof, wherein said ligand binding domain is defined by a plurality of structure coordinates of <u>a crystalline form</u> of the ligand binding domain of a FXR molecule or a fragment thereof,

wherein said plurality of structure coordinates are derived from X-ray diffraction data obtained from crystals of said FXR molecule or molecular complex or a homologue of said FXR molecule or molecular complex; and

(b) determining the ability of said test compound to modulate the activity of said FXR molecule in the optional presence of a known FXR agonist.

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- (Original) A method according to claim 19, wherein said plurality of structure coordinates are set forth in Appendix 1, or a portion thereof sufficient to define the points of interaction between said ligand binding domain and a ligand therefor.
  - 21. (Withdrawn) A compound identified by the method of claim 19.
- (Withdrawn) A pharmaceutical composition comprising a compound identified by the method of claim 19 and a pharmaceutically acceptable carrier therefor.
  - 23.-30. Cancelled.
- (Withdrawn; currently amended) A method for determining whether a test compound is capable of binding to the ligand binding domain of a farnesoid X receptor (FXR) molecule, said method comprising:
  - (a) determining the points of interaction between a <u>crystalline form of</u> the ligand binding domain of a FXR, and one or more known ligand(s) therefor; and
  - (b) analyzing said test compound to determine whether similar points of interaction exist between said test compound and said ligand binding domain.
- 32. (Withdrawn) A method according to claim 31, wherein step (a) utilizes a plurality of structure coordinates derived from X-ray diffraction data obtained from crystals of said FXR molecule or molecular complex or a homologue of said FXR molecule or molecular complex to define said points of interaction.
- (Withdrawn) A method according to claim 32, wherein said structure coordinates
  are set forth in Appendix 1, or a portion thereof sufficient to define the points of interaction
  between said ligand binding domain and said ligand(s).
  - 34.-37. Cancelled.